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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/020,888	12/19/2001	Rudolf Rigler	100564-00042	8814

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ROTHWELL, FIGG, ERNST & MANBECK, P.C.
1425 K STREET, N.W.
SUITE 800
WASHINGTON, DC 20005

EXAMINER

KENEDY, ANDREW A

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 03/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/020,888

Applicant(s)

RIGLER ET AL.

Examiner

Andrew A. Kenedy

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11 is/are pending in the application.
- 4a) Of the above claim(s) 6-10 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-5 and 11 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☒ Claim(s) 1-11 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on ____ is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date ____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: ____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Specie A in the response of April 11, 2003, is acknowledged. Claims 6-10 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected Specie B, there being no allowable generic or linking claim.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because: Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

Specification

The disclosure is objected to because of the following informalities: The word "Stretched" appearing on page 8, line 5 of the specification appears to be a misspelling of the word "Stretched". Appropriate correction is required.

Claim Rejections - 35 USC § 112

Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for molecular event sequences such as fluorescence emission by a molecule, does not reasonably provide enablement for an event sequence such as a series of lightning strikes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

A series of lightning strikes during a thunderstorm is an event sequence encompassed by Claims 1-3. Given the occurrence of lightning strikes at the same location in Central Park five minutes ago, one minute ago, and just now, I would like to determine whether that particular series of lightning strikes is a memory driven event sequence or not. The claimed invention and accompanying disclosure do not appear to provide the necessary guidance or positive active steps required to determine whether the above example represents a memory driven event sequence. The instant invention cannot be used to determine whether the above event sequence is memory driven or not, because the above event sequence by itself does not contain enough information. The instant invention only appears to work when one has obtained measurements of multiple repetitions of a particular event sequence, something that is required in order to calculate the probabilities necessary for computing the first and second order autocorrelation functions disclosed on pages 4-5 of the specification.

Therefore, while the Applicants' invention may be enabled for highly repetitious event sequences that can be measured repeatedly over a short time scale, such as events at the molecular level like fluorescence, the invention is not enabled for infrequent event sequences that occur over a long time frame and for which multiple past observations of the precise event sequence phenomenon are not readily available.

Claims 1-5 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In Claim 1, the phrase "within experimental error" is indefinite as to the particular threshold or confidence interval used to define the metes and bounds of the acceptable error range, thereby rendering the scope of the claim uncertain as to what applicants consider to be within experimental error.

In Claim 1, the criteria for making the determination of whether an event sequence is memory driven is inconsistent with that of the disclosure on page 6 of the specification and is therefore confusing. Specifically, the claim states the an event sequence is memory driven if the second order autocorrelation function equals the product of the first order autocorrelation functions. The specification states exactly the opposite. The same problem exists with the criteria for determining whether an event is non-memory driven.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1 and 2 are rejected under 35 U.S.C. 102(e) as being anticipated by Carson et al. (US 6078872 A).

With respect to Claim 1, Carson et al. teaches a method for measuring properties of a system with memory where first order correlation functions, S_a and S_b , are obtained for each of two different measurement periods, and a second order correlation function, S_2 , is computed as the product of the two first order correlation functions: $S_2 = S_a S_b$ (see at least Claim 1; col. 1, lines 61-67; col. 2, lines 38-49; col. 2, lines 1-16; col. 3, lines 50-57; col. 5, lines 3-46; col. 6, lines 43-45; and Fig. 1A-B). Carson et al. further teaches that the correlation function is an autocorrelation function when two measurements differ only in the times at which they were made (col. 2, lines 22-25). With respect to Claim 2, Carson et al. teaches that when dealing with quantum mechanical applications, the measured quantities (the first order autocorrelation functions used to compute the second order autocorrelation function) are expectation values (see at least col. 24, lines 50-60).

Since Carson et al. teaches that the above second order autocorrelation function computation is valid for memory driven event sequences (see at least col. 5, lines 27-42), one of ordinary skill in the art would have implicitly understood that if the computation did not produce a result that was within the bounds of experimental error for a measured event sequence, the event sequence could not be memory driven.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Carson et al. (US 6078872 A) in view of Dhingra et al. (*Engineering Optimization*, 1995).

Carson et al. is applied as above. Carson et al. does not teach that the degree of memory of the system can be quantified by a non-Markovian function.

Dhingra et al. teaches the use of a non-Markovian function in solving memory-based problems. Specifically, Dhingra teaches using a non-Markovian function to classify certain events of an event sequence as forbidden (quantification of a degree of memory of the system) (see at least the abstract).

It would have been obvious for one of ordinary skill in the art to combine the teachings of Dhingra et al. with Carson et al. to quantify the degree of memory of the system by a non-

Markovian function, since Dhingra et al. teaches that the optimum solutions obtained by using non-Markovian functions outperform the optimum solutions obtained using other techniques (see at least the abstract).

Claims 4, 5 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carson et al. (US 6078872 A) in view of Qian (*Biophysical Chemistry*, 1990).

Carson et al. is applied as above. With respect to Claim 11, Carson et al. further teaches that autocorrelation functions can be applied to states of oscillators, such as mechanical oscillators or electromagnetic fields (oscillating processes) (see at least col. 4, lines 7-13).

Carson et al. does not teach autocorrelation functions applied to a sequence of fluorescence events observed in a confocal microscope to determine whether an event sequence is memory driven or not, or to specifically determine whether the fluorescence event sequence is due to an event sequence from a molecule and thus memory driven, or if the event sequence is due to background noise and thus non-memory driven.

Qian teaches first and second order autocorrelation functions applied to an event sequence of molecules observed by fluorescence laser confocal microscopy (see at least the abstract; and pg. 53, col. 1, paragraph 2), to determine whether the observed fluorescence is due to a molecule (memory driven event) or is just background noise (non-memory driven event).

It would have been obvious to combine the teachings of Qian with Carson et al. to determine whether fluorescence events observed in a confocal microscope are memory driven or non-memory driven, since Qian teaches that first- and second-order autocorrelation functions can

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be used to completely exclude noise from a microscopic fluorescence signal when viewing molecules (see at least pg. 53, col. 1, paragraph 2; and pg. 50, col. 1, paragraph 1).

Made of Record

Prior Art made of record which discloses various aspects of applicants' instant invention but was not relied upon:

Lu et al. ("Single-molecule spectral fluctuations at room temperature", *Nature*, Vol. 385, 9 January 1997, pg. 143-146) teaches autocorrelation functions as applied to fluorescence microscopy; Lu et al. ("Single-Molecule Enzymatic Dynamics", *Science*, Vol. 282, 4 December 1998, pg. 1877-1882) teaches autocorrelation functions as applied to fluorescence microscopy; Wennmalm et al. ("Conformational fluctuations in single DNA molecules", *PNAS*, Vol. 94, September 1997, pg. 10641-10646) teaches autocorrelation functions as applied to fluorescence microscopy; Edman et al. ("Conformational transitions monitored for single molecules in solution", *PNAS*, Vol. 93, June 1996, pg. 6710-6715) teaches autocorrelation functions as applied to fluorescence microscopy.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew A. Kenedy whose telephone number is (571)-272-0574. The examiner can normally be reached on Monday-Friday 9:00am-5:00 pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571)-272-0722. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A.A.K. March 17, 2004

Marianne P. Allen
MARIANNE P. ALLEN
PRIMARY EXAMINER
3/22/04
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